5XCC0 Biopotential and Neural Interface Circuits

Introduction to biopotential and neural interfaces & other healthcare applications

Pieter Harpe

Outline

- Introduction
- Biopotential interfaces
- Neural interfaces
- Other healthcare applications
- Examples from TU/e
- Summary

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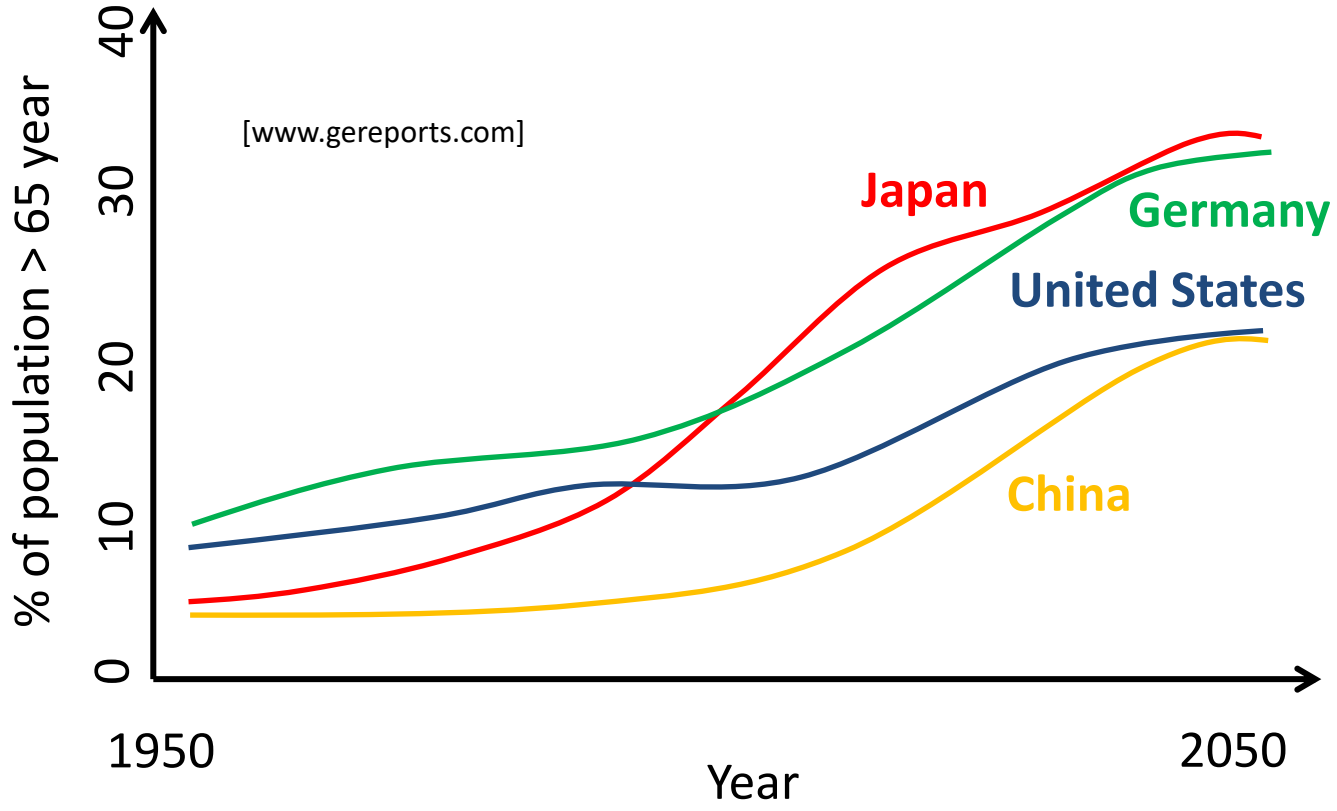
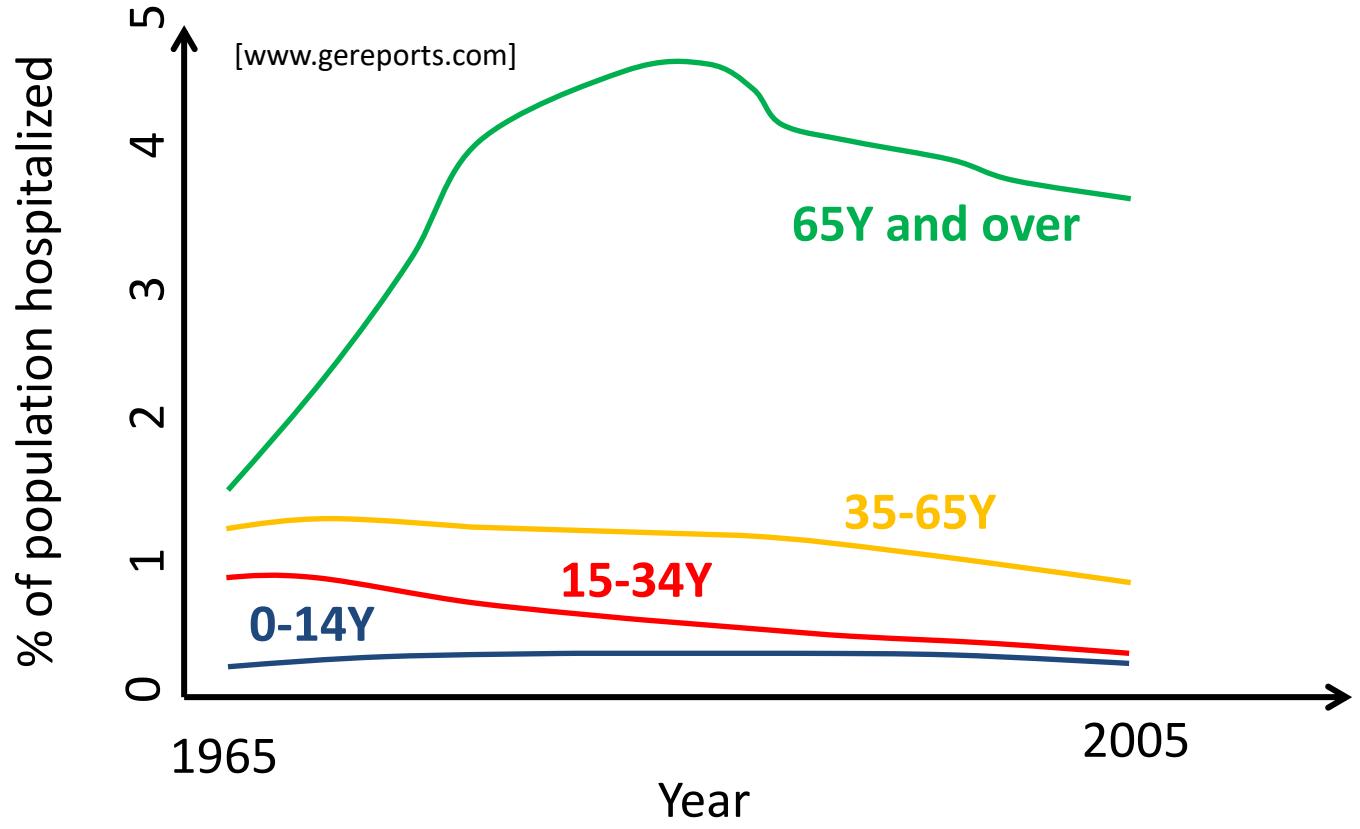
Worldwide Ageing of Population

- Society is ageing (worldwide)



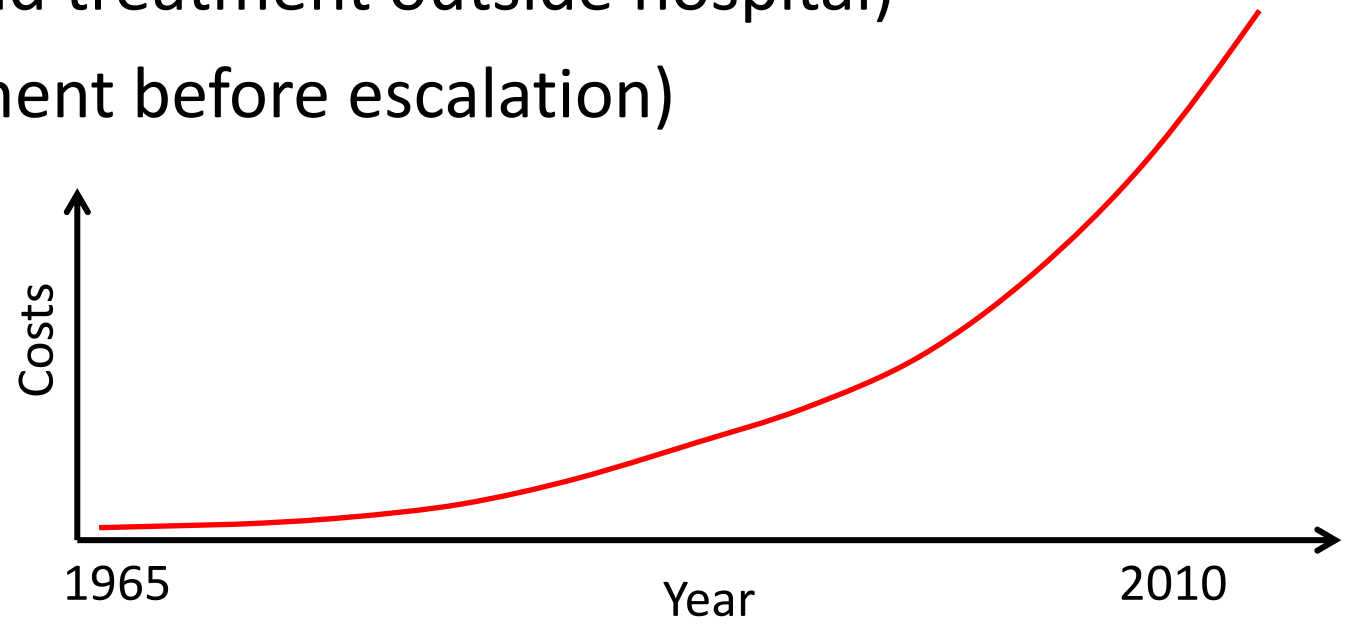
Hospitalization per Age Category

- 65+ category requires more frequent hospitalization



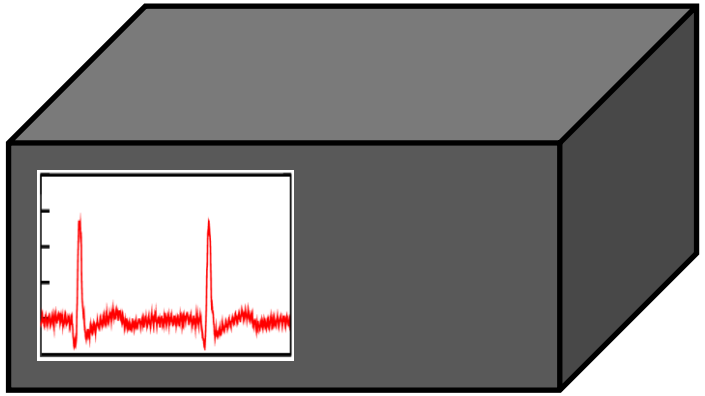
Healthcare Costs

- Ageing & increased hospitalization
- Rapid increase in costs & required hospital manpower
- Developments in healthcare
  - Mobile care (monitor and treatment outside hospital)
  - Prevention (early treatment before escalation)

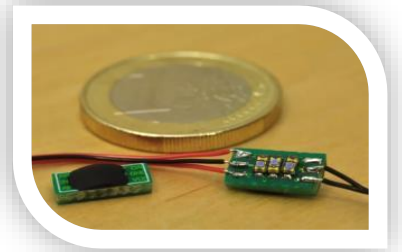


Example: ECG Monitor

Past: large stationary equipment



Present: mm^2-sized integrated circuits

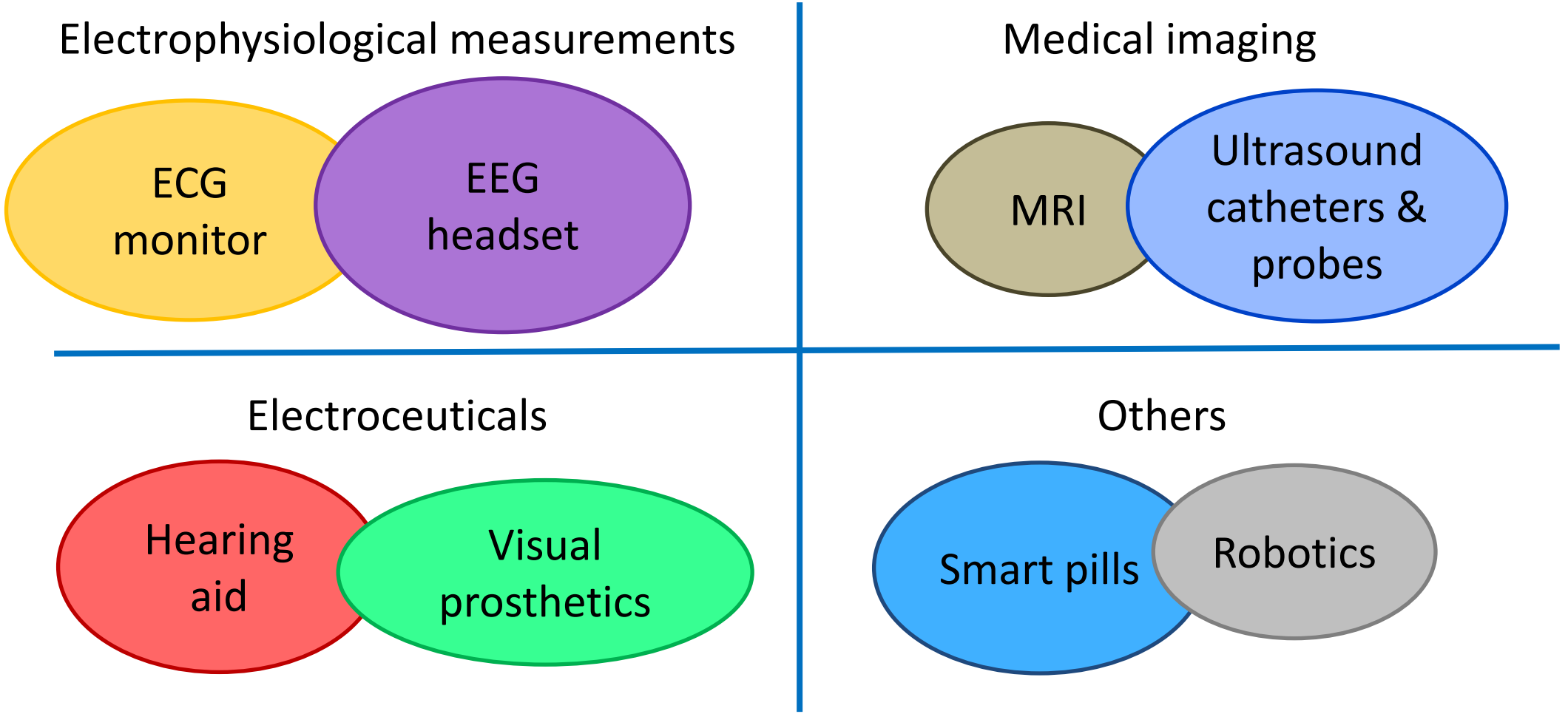


[Harpe, ISSCC 2015]

- Large, heavy
- Mains powered
- Expensive

- Small, portable
- Low-power
- Cheap
- New functionalities (radio, network, …)

Biomedical Applications



- Note: use Google to search for some examples!

Emerging Applications

- Wearable devices
- Implants
- Catheters
- Intelligent pills & robotics

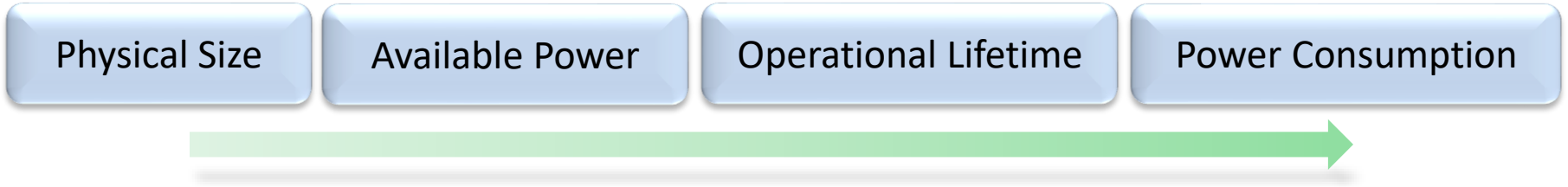
- Small devices
  - Integrated circuit (IC) design AND low energy consumption → Small form factor, Longer operational time, Less heating

Size and Impact on Power Consumption

- Example: Cardiac pacemaker
  - Battery takes substantial space
  - More pronounced in smaller systems

https://www.youtube.com/watch?v=jAAAQu6CzoA

https://www.youtube.com/watch?v=M_FBDUzxwGc

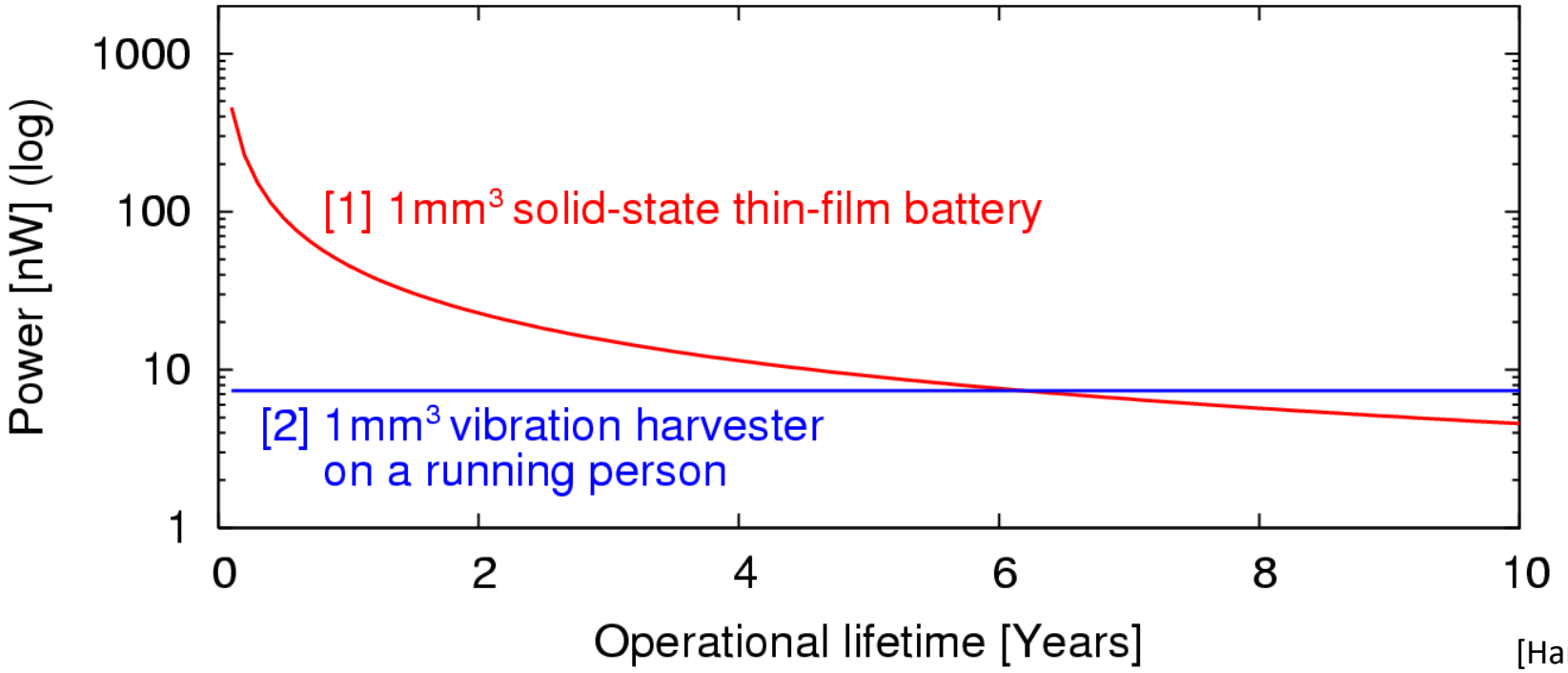


- Miniature size → Extremely low power electronics

https://www.youtube.com/watch?v=M9KypHkqpTM

State-of-the-art Batteries / Harvesters

- For multi-year lifetime: $P_{avg} \approx 10nW/1mm^3$
  - 10nW for $1mm^3$
  - 10µW for $1cm^3$



[Harpe, ISSCC 2015]

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Electrophysiological Measurements

- Measurement of electrical activity/properties of cells and tissue

Biopotentials: electrical voltages generated by physiological processes in the body

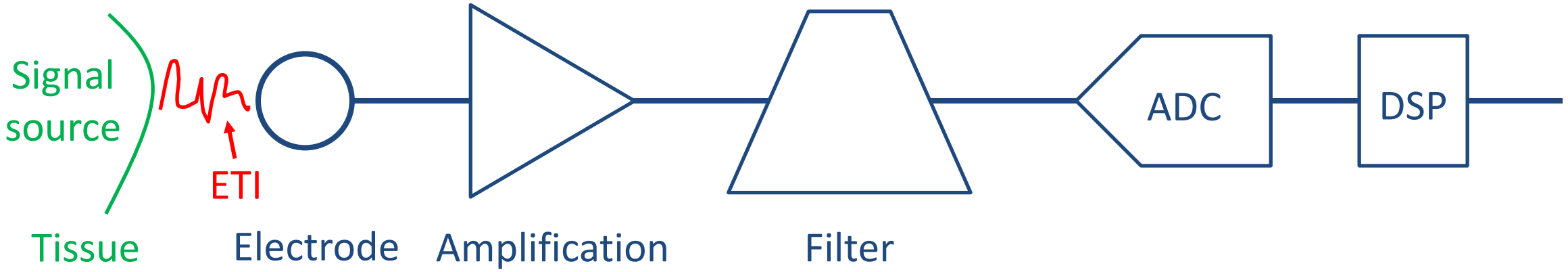
Biopotential interface: circuit that measures biopotentials

Measurement	Amplitude Range	Frequency Range
Electrocardiography (ECG)	0.5 – 4mV_{pp}	0.01 – 250Hz
Electroencephalography (EEG), on scalp	5 – 300μV_{pp}	DC – 150Hz
Electrocorticography (ECoG), in brain	10 – 5000μV_{pp}	DC – 150Hz
Electrogastrography (EGG), on skin	10 – 1000μV_{pp}	DC – 1Hz
Electrogastrography (EGG), on stomach	0.5 – 80mV_{pp}	DC – 1Hz
Electromyography (EMG)	0.1 – 5mV_{pp}	DC – 10kHz
Electrooculography (EOG)	50 – 3500μV_{pp}	DC – 50Hz
Electroretinography (ERG)	0 – 900μV_{pp}	DC – 50Hz
Nerve potentials (AP/LFP)	0.01 – 5mV_{pp}	0.5 – 6000Hz
Galvanic skin response (GSR)	1 – 500kΩ	0.01 – 1Hz

[Medical Instrumentation, J.G. Webster]

- Small, variable amplitudes & Low frequencies

Typical Biopotential Interface

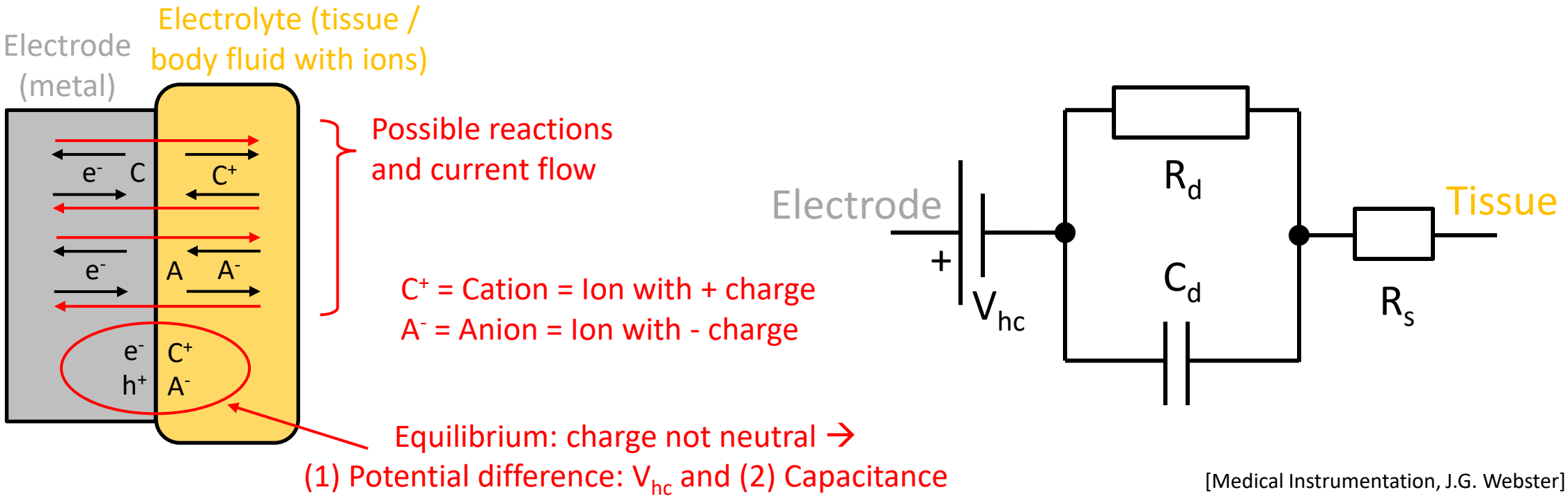


- ETI: electrode tissue interface
- Amplification: because the signal is usually small
- Filter: to remove DC, to minimize disturbance, to satisfy Nyquist
- ADC: to digitize the analog signal
- DSP: for (advanced) signal processing, storage, etc.

Wearable Devices vs Implants

Wearable	Implant
All electronics outside the body	Electronics placed inside the body
Small size and low power preferred	Small size and low power required
Short to long term operation	Very long term operation (>> years)
Skin electrodes to capture signal	Electrodes directly contact internal tissue
Smaller signal amplitude, less spatial info	Higher signal amplitude, more spatial info
More susceptible to environmental noise	Less susceptible to environmental noise
Avoid skin irritation, allergic reactions, etc.	Requires biocompatibility and stability (prevent toxicity, material diffusion, chemical reactions)

Electrode-Tissue Interface (ETI)

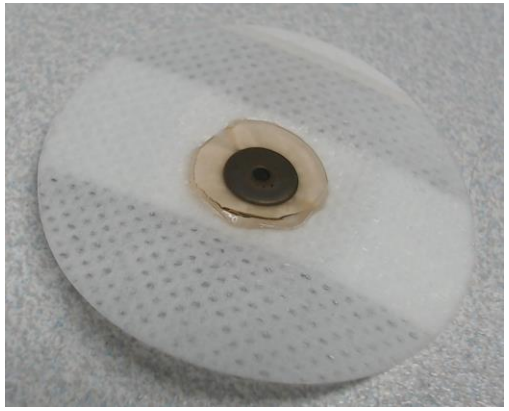


[Medical Instrumentation, J.G. Webster]

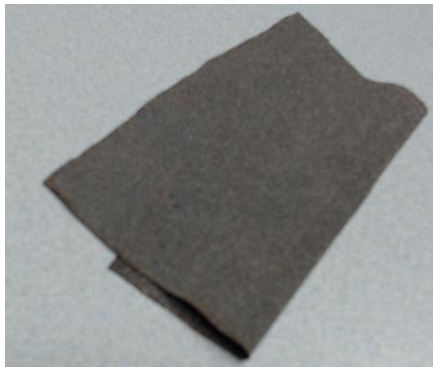
- V_{hc}: Half-cell potential (material dependent) due to equilibrium of chemical reactions
- C_d: Capacitance of the double layer of charge in the electrode-electrolyte interface
- R_d: Leakage resistance across the double layer
- R_s: Resistance of the electrolyte
- Parameters are non-constant, non-linear, temperature dependent, area dependent, etc.

(Skin) Electrode Types

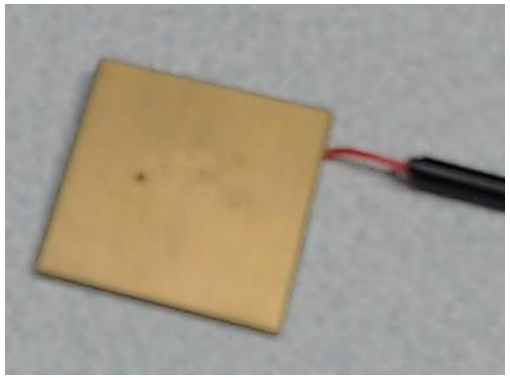
Gel / Wet



Dry



Capacitive



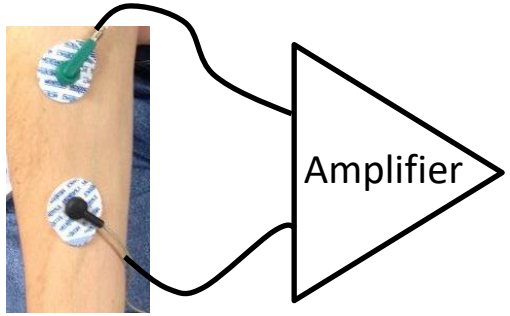
- Gel: conductive gel creates Galvanic connection: lowest and reliable impedance, requires skin preparation
- Dry: electrode without gel applied to skin: higher impedance, less reliability, easy to apply
- Capacitive: Galvanically isolated electrode (capacitive coupling): highest impedance, best comfort

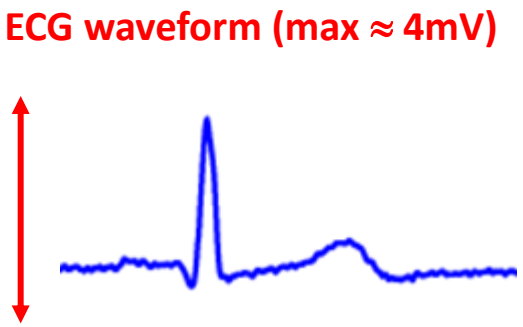
Measurement Challenges

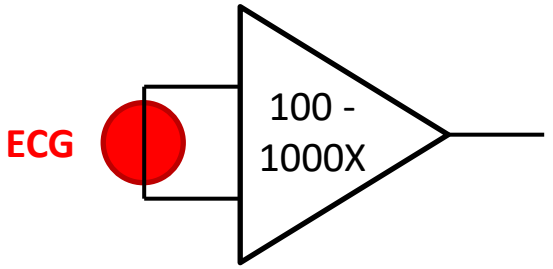
- Small signal amplitudes
- Relatively large (and uncertain) ETI impedance
- Large disturbances
  - Powerline interference
  - Motion artifacts
  - Interference: e.g. EOG (3.5mV) obstructing EEG (5μV)
- (Close-to-)DC information needed

Small Signal Amplitudes

- High gain required to amplify the small signal of interest
- Low “input-referred” noise of the electronics
- Signal is easy to get lost in interference, artifacts, etc.

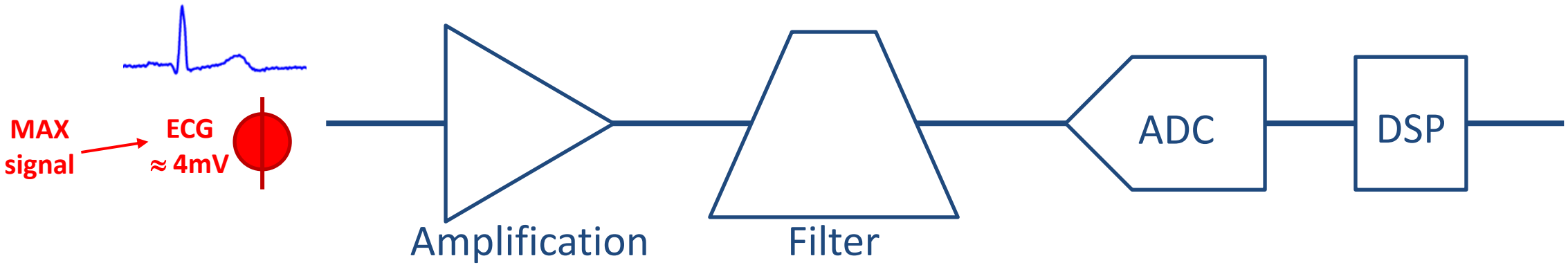






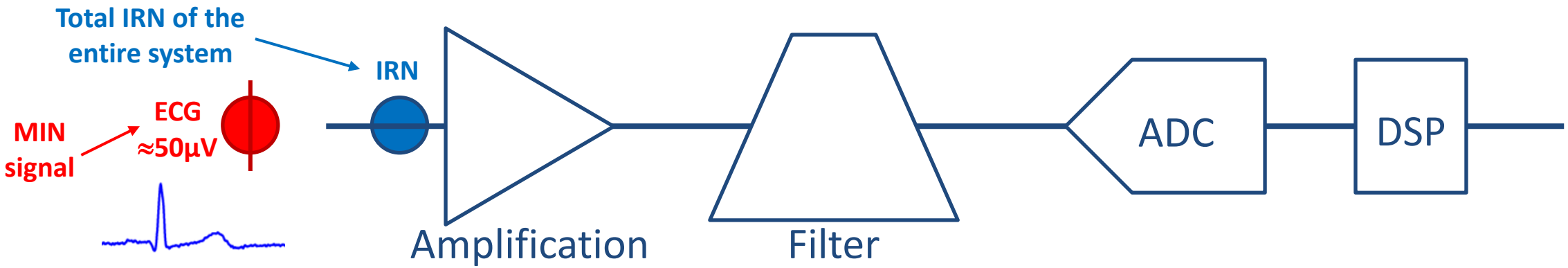
Required Gain

- Signal of interest is usually small (µV to mV level)
- Filters & ADCs are most *efficient* when signals are relatively large (near the full-scale of these circuits), (100's mV to V level)
- To bridge this gap, we need gain. Trade-off:
  - Minimum signal amplitude should be detectable by the system
  - Maximum signal, interference, DC, etc., should not saturate the system



Input-Referred Noise

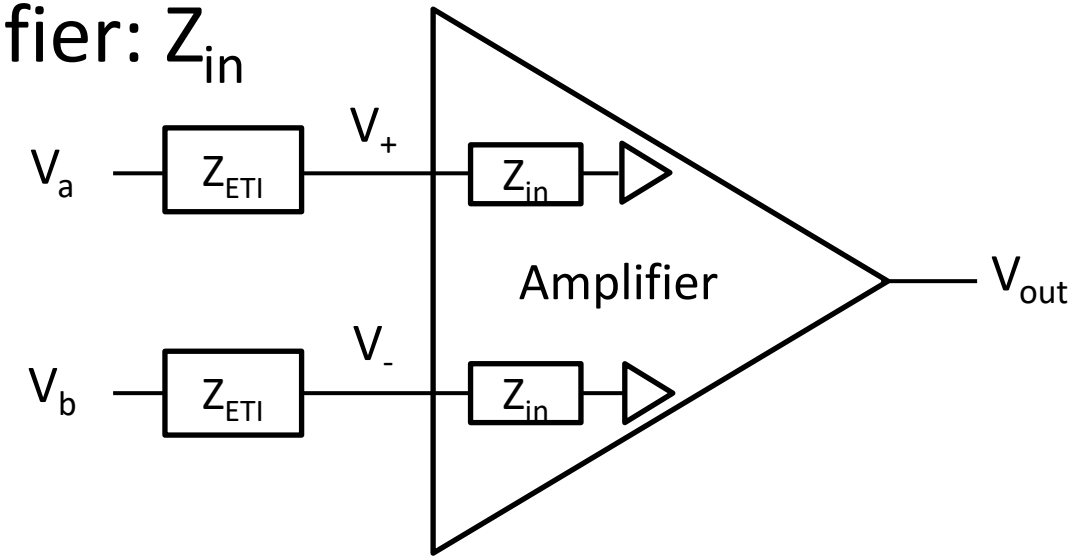
- All electronic circuits add (random) noise
  - Thermal noise, 1/f noise, quantization noise
- Note: ETI, environment, tissue also add noise
- The total input-referred noise (IRN) defines the sensitivity of the system, and should be smaller than the smallest signal that you want to detect



ETI Impedance

- Electrode-tissue impedance: Z_{ETI}
- Finite input impedance of the amplifier: Z_{in}

$$V_+ = V_a \cdot Z_{in} / (Z_{ETI} + Z_{in})$$
$$V_- = V_b \cdot Z_{in} / (Z_{ETI} + Z_{in})$$



- Signal at amplifier input ($V_+ - V_-$) is attenuated compared to signal at the source ($V_a - V_b$)
- Solution: $Z_{in} >> Z_{ETI}$ to minimize loss
  - If Z_{in} and/or Z_{ETI} is capacitive, this loss might be frequency dependent

Exercise 1: ETI Impedance

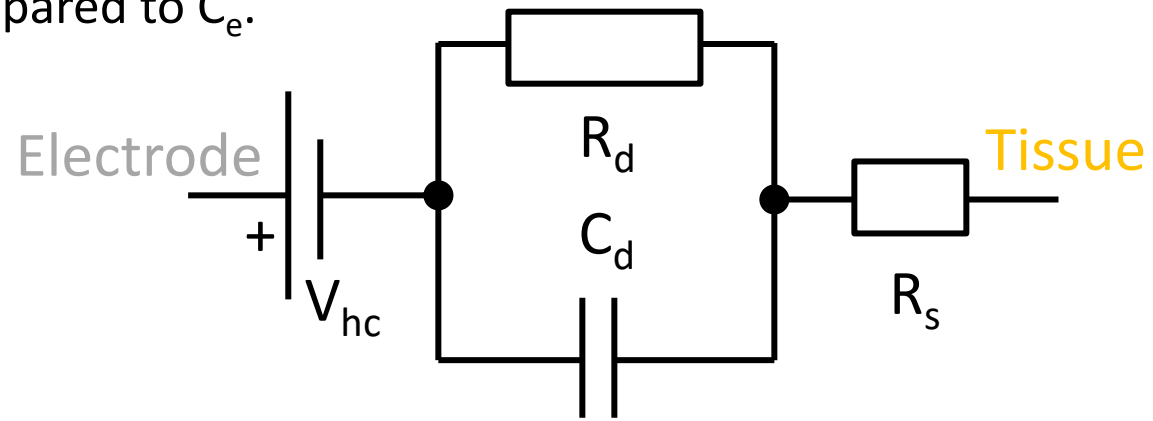
Suppose an ETI is given with certain values for C_d, R_d, R_s

a) If a wet electrode is used, what do you expect to happen with the values of C_d, R_d, R_s if we double the area A of the electrode? You may give a qualitative answer.

b) If we use a capacitive electrode, a series capacitor C_e should be added to the model to mimic its capacitance. How does C_e depend on the area A of this electrode and the thickness d of its isolation?

c) What value (numeric) do you expect for C_e if the electrode area is $16cm^2$, and the isolation material is a 0.3mm thick cotton fabric?

d) How large should the amplifier input impedance be (numeric, in ohms) if the signal loss should be less than 10% at a frequency of 100Hz if we use a C_e as calculated in question c)? You may assume that Z_{ETI} is negligible compared to C_e.

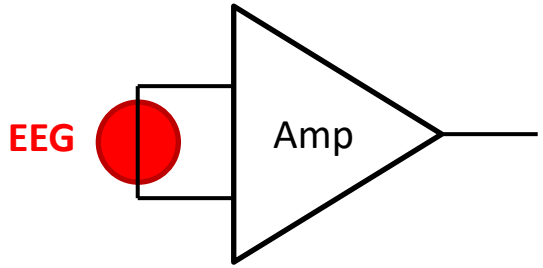


Exercise 2: Gain and Noise

Suppose we want to record an EEG signal. An amplifier with gain A is connected to two recording electrodes. The maximum expected peak amplitude of the EEG signal is $0.4mV_{pp}$, the smallest detail we want to detect is $2\mu V_{rms}$. We expect a powerline interference of max $50mV_{pp}$ at the amplifier output. Besides that, differential disturbance signals up to $2mV_{pp}$ can be expected at the amplifier input. The output range of the amplifier is $1.2V_{pp}$.

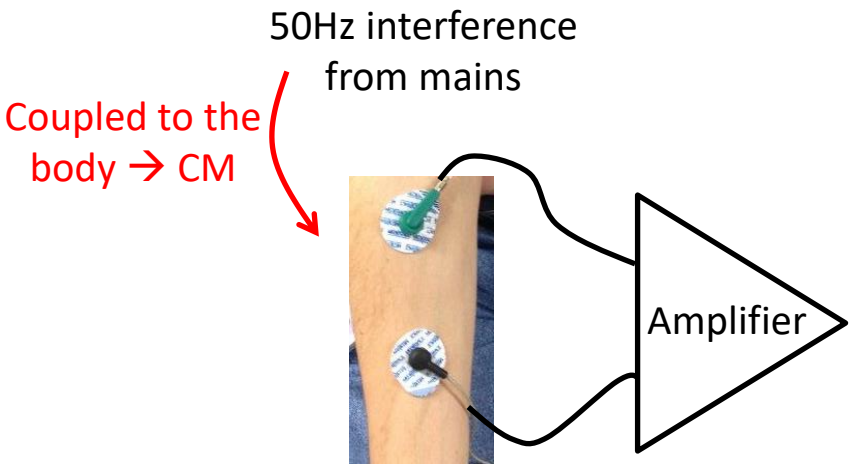
a) What is the gain A that you would choose for the amplifier?

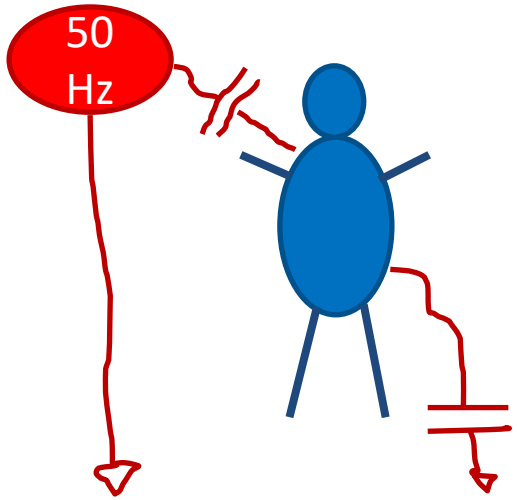
b) What should be the IRN of the amplifier?

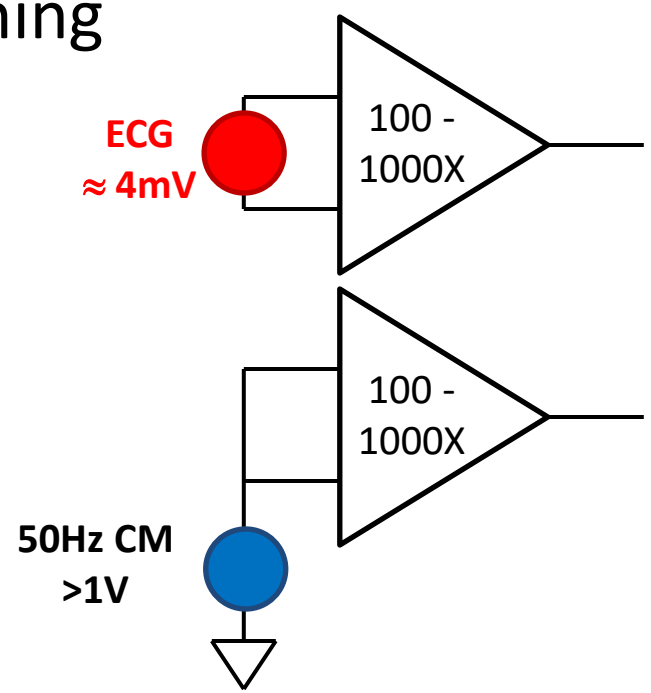


Powerline Interference

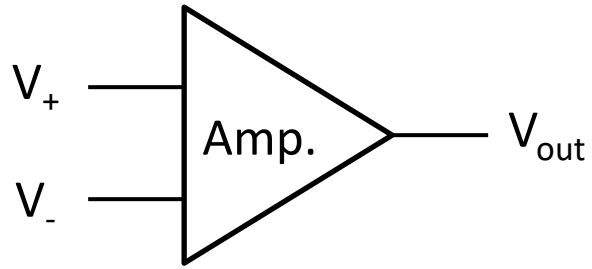
- Powerline (50Hz/60Hz) Common-Mode (CM) disturbance
- Signal of interest (ECG) is a differential signal; external interference can show up as a common-mode signal
  - Large CMRR needed AND perfect differential matching
  - CM may be outside supply range







Common-Mode Rejection Ratio (CMRR)



$$V_{out} = A_d (V_+ - V_-) + \tfrac{1}{2} A_c (V_+ + V_-)$$

A_d : Differential gain

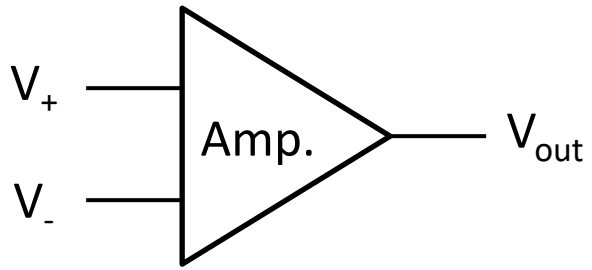
A_c : Common-mode gain (ideally 0)

$$CMRR = 20 \log_{10} (A_d / |A_c|)$$

- Notes:
  - There are various (slightly different) CMRR definitions
  - CMRR looks at small-signal behavior
    - If CM disturbance is very large, the amplifier might saturate, and the small-signal model does not hold

Impact Finite CMRR Amplifier

- Suppose the amplifier has an input signal:
  - Differential EEG of 100µV
  - Common-mode powerline interference of 100mV



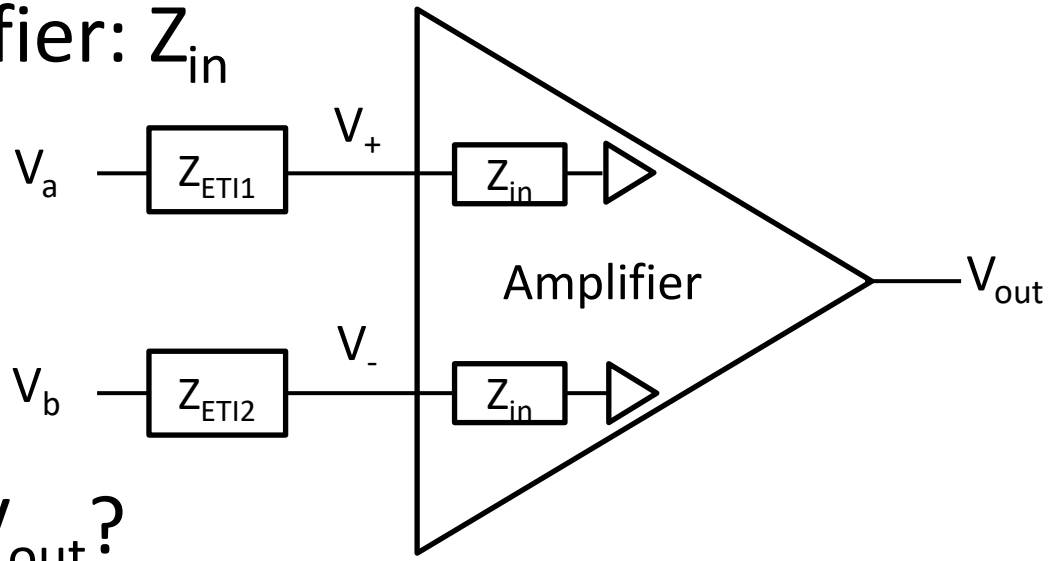
- Further assume that A_d = 400V/V, CMRR = 60dB

- Then: A_c = 0.4V/V
  - V_{out} will contain a 40mV EEG signal + a 40mV powerline signal
  - Extra dynamic range is needed (the system should not saturate when processing 40mV signal + 40mV disturbance, even though the useful information is only 40mV)

Impact Electrode Mismatch and Input Impedance

- Electrode mismatch: $Z_{ETI1} \neq Z_{ETI2}$
- Finite input impedance of the amplifier: Z_{in}

$$V_+ = V_a \cdot Z_{in} / (Z_{ETI1} + Z_{in})$$
$$V_- = V_b \cdot Z_{in} / (Z_{ETI2} + Z_{in})$$
$$V_{out} = A_d (V_+ - V_-),\ A_c = 0$$



- What is the impact of input CM on V_{out}?

$V_a = V_b = V_{cm} \rightarrow V_{out}$ becomes f (V_{cm})

→ It can be shown that

$$CMRR \approx 20 \log_{10} \{Z_{in} / \Delta Z_{ETI}\}$$

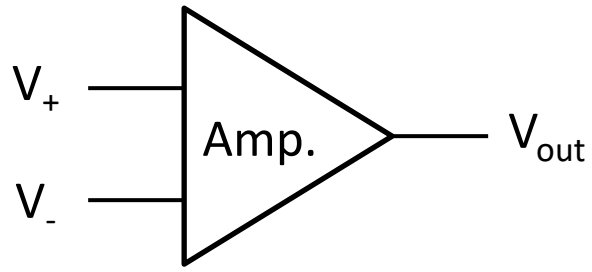
- This issue is often worse than the amplifier CMRR
- Solutions:
  - Minimize electrode mismatch (hard to control)
  - Maximize Z_{in}

Exercise 3: Amplifier CMRR

A given amplifier has a differential gain A_d of 100 V/V. Powerline interference creates a 50mV CM signal at the amplifier input.

a) What is the maximum tolerated common-mode gain A_c, such that the powerline interference at the output of the amplifier is not greater than 1mV?

b) What is the required CMRR of this amplifier?



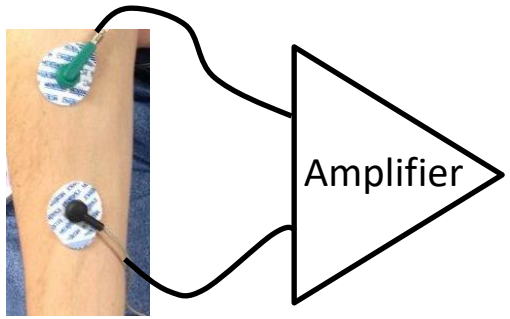
Exercise 4: Electrode Mismatch CMRR

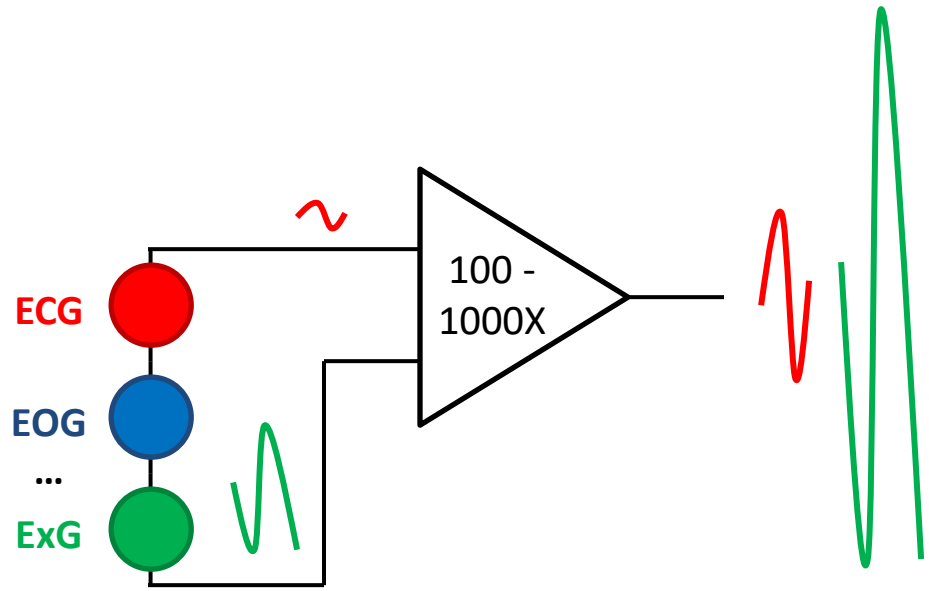
a) On slide 28, it was claimed that CMRR ≈ 20 $\log_{10}$ $\{Z_{in} / \Delta Z_{ETI}\}$. Note that this equation is an approximation. Can you derive (prove) this equation? What is the assumption that you need to make to come to this approximation?

b) Suppose we have two electrodes with an impedance of 100kΩ and 140kΩ, respectively. What should the input impedance of the amplifier be to reach a CMRR of 80dB?

Motion Artifacts, Interference

- Large Dynamic Range needed
- Spatial discrimination
- Frequency-domain filtering
- Time selection
- Advanced DSP



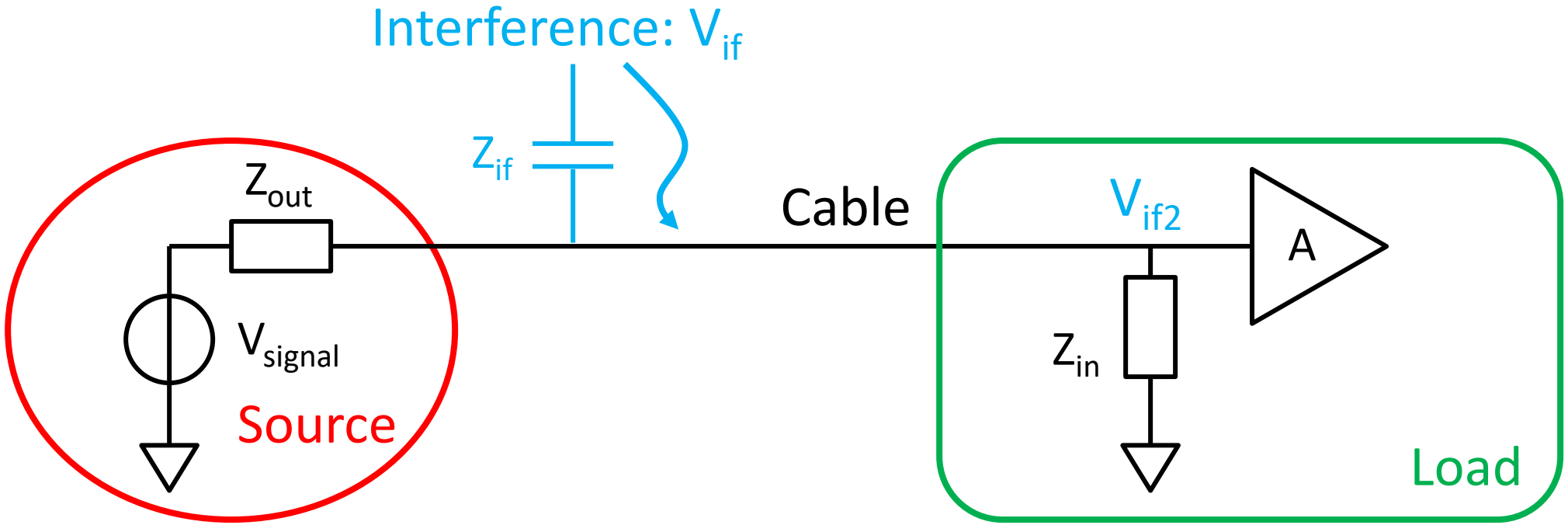


Dynamic Range of the System

- Dynamic Range: largest signal versus the smallest signal that can be processed by the system:
  - Largest signal: maximum amplitude that does not saturate the system
    - This should include not only the signal of interest, but also disturbances (DC offset, powerline and other CM interference, differential disturbances, etc.)
  - Smallest signal (sensitivity): minimum amplitude that can be detected, i.e. the noise-level of the system
    - This is defined by the IRN of the system
- Usually, the DR is expressed in dB: $DR = 20 \log_{10} (V_{max} / V_{min})$
  - Note that V_{min} and V_{max} thus need the same unit (!)

Interference Sensitivity

- Cables are sensitive to pick up interference from the environment
  - High impedance nodes are more sensitive to pick up interferences



$Z_{cable} = Z_{in} // Z_{out}$ (!). Usually: $Z_{in} >> Z_{out} \rightarrow Z_{cable} \approx Z_{out} \rightarrow V_{if2} = V_{if} \cdot Z_{cable} / (Z_{cable} + Z_{if})$

Exercise 5: Dynamic Range

Suppose we want to record an EEG signal. An amplifier with gain A is connected to two recording electrodes. The maximum expected peak amplitude of the EEG signal is $0.4mV_{pp}$, the smallest detail we want to detect is $2\mu V_{rms}$.

a) What is the required dynamic range of the amplifier?

Now, we add several disturbances: We expect a CM powerline interference of max $100mV_{pp}$, while the CMRR of our amplifier is known to be 60dB. Besides that, differential disturbance signals up to $2mV_{pp}$ can be expected.

b) What is now the required dynamic range?

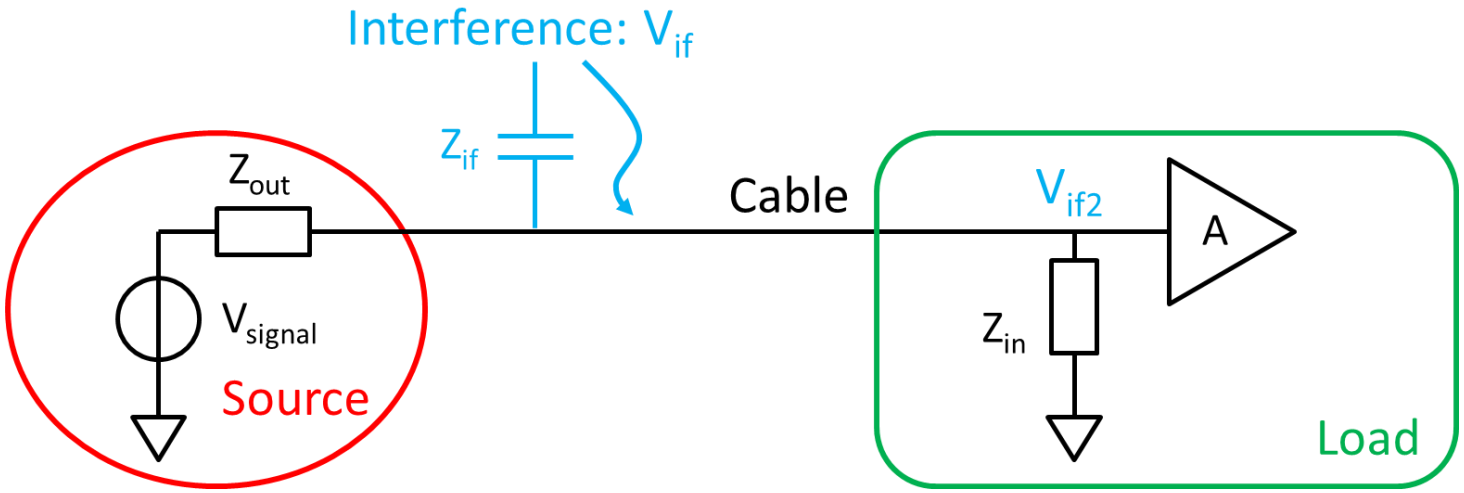
Exercise 6: Interference Sensitivity

Given the system below, you may assume that Z_{out} is 500kΩ, Z_{in} is 5MΩ, Z_{if} is caused by a 2pF capacitance, V_{if} is 2V, and the signal bandwidth of interest is from 1Hz up to 1kHz.

a) Do interferences at higher or lower frequency have more impact on the system? Why?

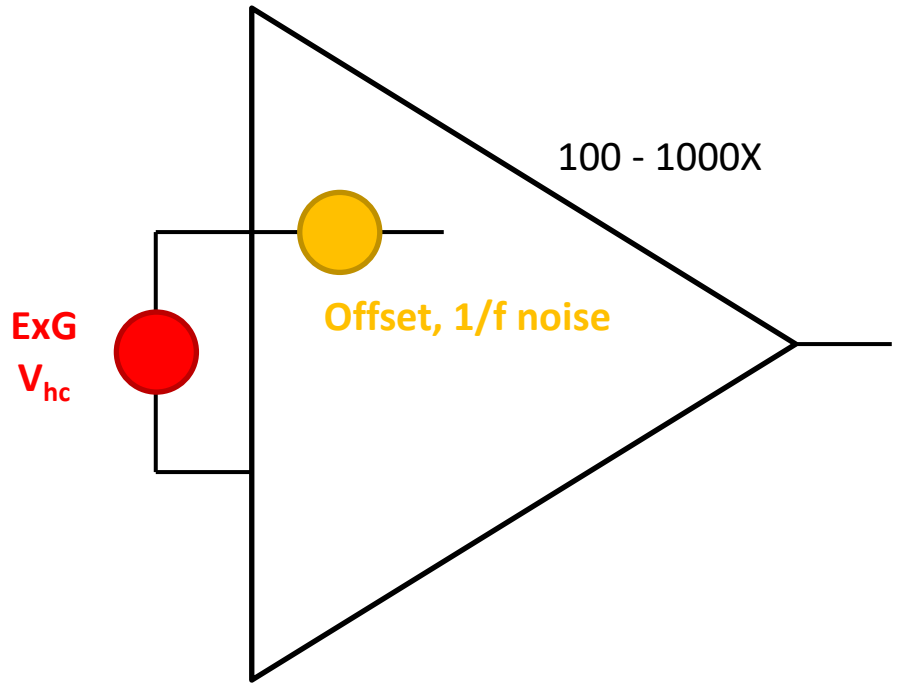
b) Calculate the amplitude of V_{if2}, assuming that V_{if} is at the worst possible frequency.

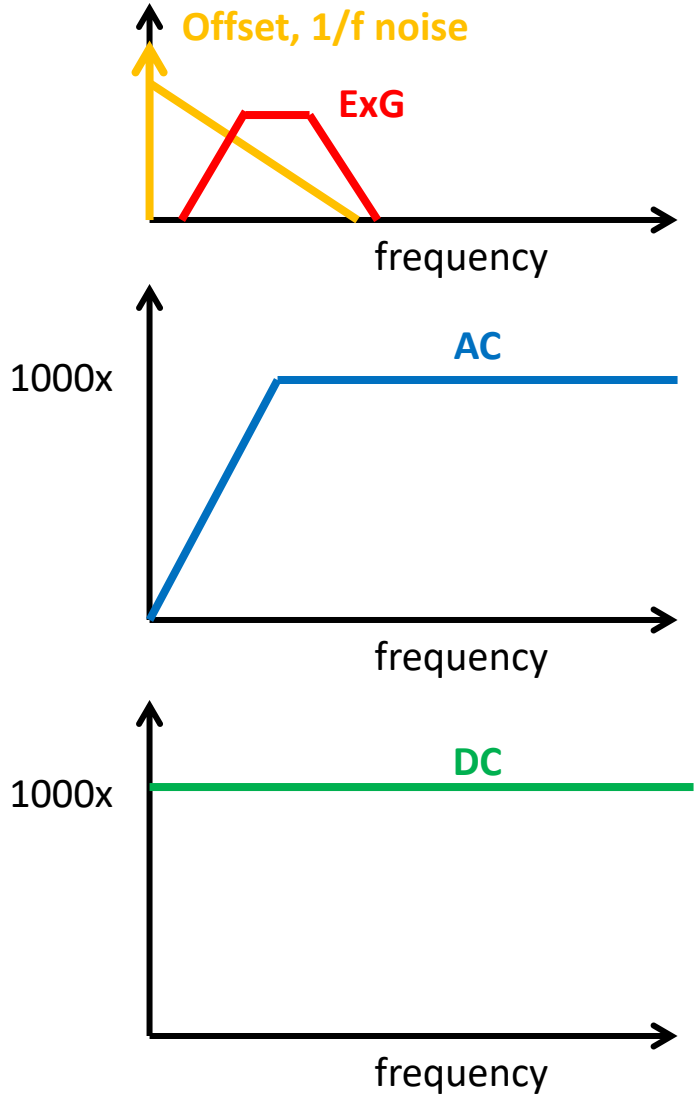
c) How much lower will V_{if2} be if we lower Z_{out} by 10x?



(Close-to-)DC Information

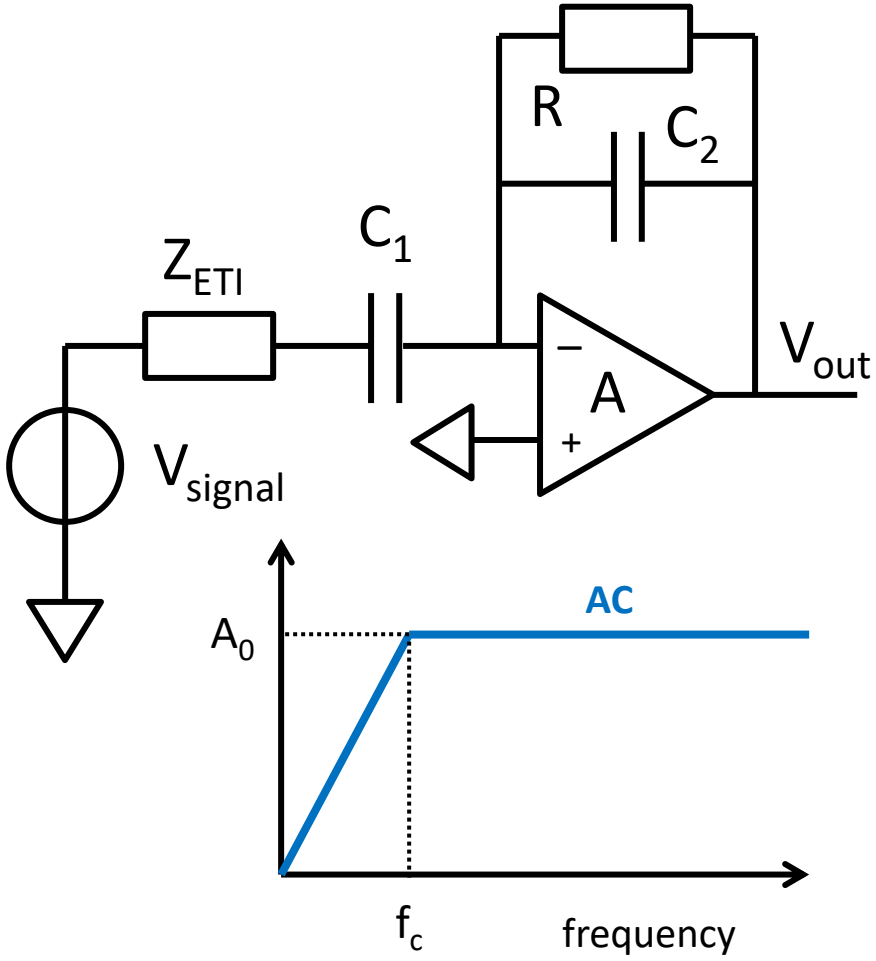
- AC-coupled: offset canceled, still low 1/f needed and very low cut-off frequency
- DC-coupled: needs low offset & 1/f noise





AC Coupling

- AC coupling should be *before* amplification, otherwise saturation
  - Gain: $A_0 = C_1 / C_2$
  - Cut-off frequency: $f_c = 1 / (2\pi RC_2)$
  - $Z_{in} = 1 / sC_1$
- Trade-off:
  - For large Z_{in} → C_1 small
  - For low f_c, high gain A_0 → C_1 large



DC Coupling

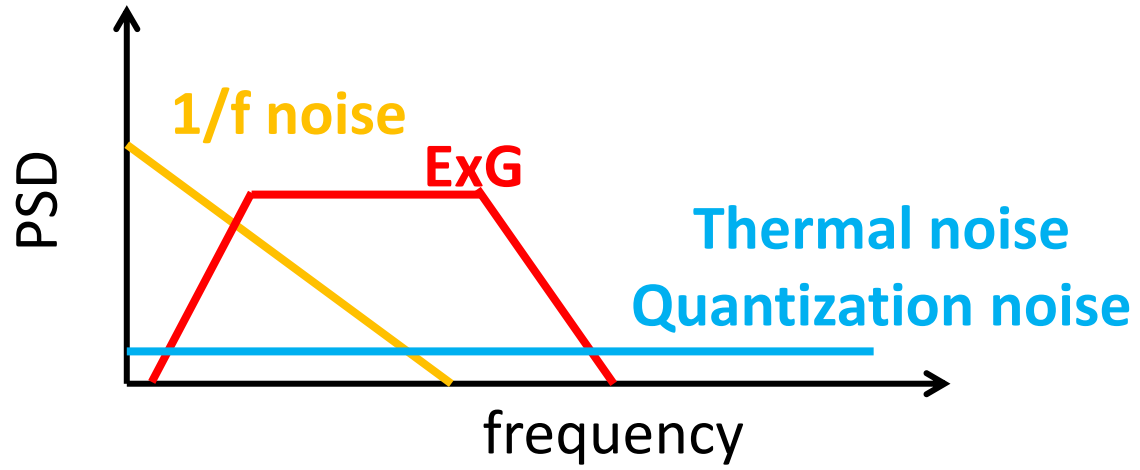
- Signals of interest: µV to mV level
  - Gain in the order of 100X to 1000X would be of interest

- DC components:
  - V_{hc}, in the order of 100's of mV. V_{hc} mismatch might be substantial
  - Amplifier offset might also be in the order of µV to mV

- DC components might limit max. gain (to avoid saturation)
  - Increased DR requirement; less gain; less efficient back-end

1/f Noise

- 1/f noise (flicker noise) has a power-spectral density (PSD) that is inversely proportional to the frequency
- ExG signals are at low frequencies too
- Often the 1/f noise is dominant compared to white noise sources



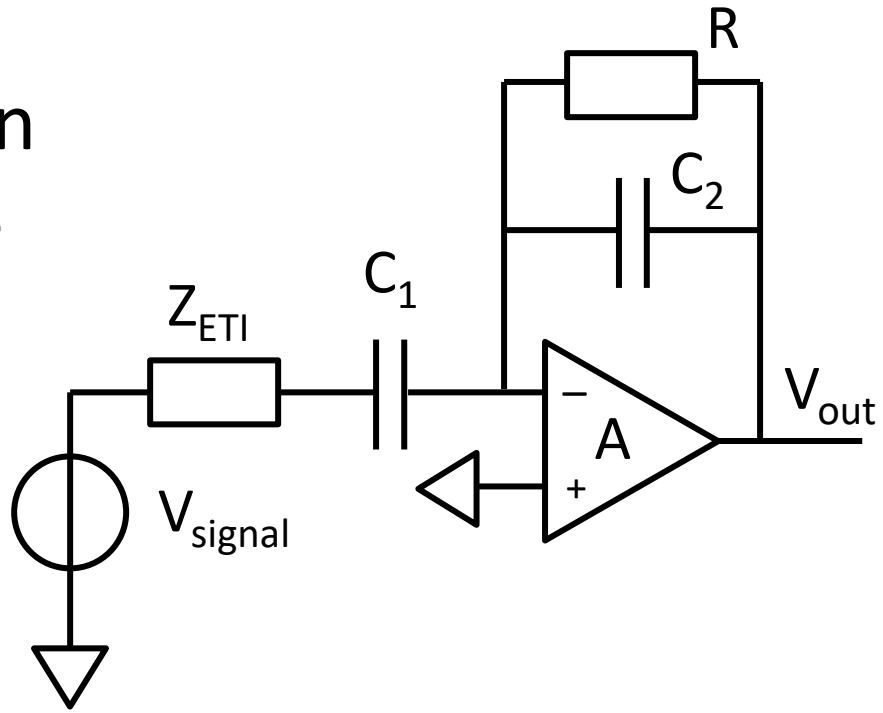
Exercise 7: AC Coupling

An AC-coupled amplifier is given. You may assume that Z_{ETI} is 500kΩ, the required gain is 100 V/V, the cut-off frequency should be below 0.1Hz. The signal loss (due to Z_{in}) should be less than 1dB in a bandwidth up to 500Hz.

a) Calculate the acceptable value of Z_{in}.

b) Determine C_1 based on question a).

c) Calculate C_2 and R.



Exercise 8: DC Coupling

Assume we have a DC coupled amplifier. Due to electrode mis-match, the half-cell potentials result in a differential DC level of up to 100mV. The signal of interest is 400µV. The amplifier has a 1V output range.

a) To support the DC level from the half-cell potential (without saturating), how much should the dynamic range be increased (in dB) compared to an AC coupled amplifier?

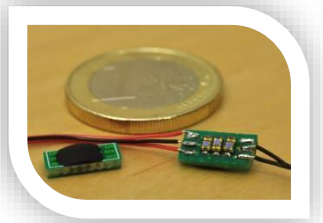
b) What is the maximum possible gain, and how does this compare to the maximum gain of an AC coupled amplifier?

ECG Monitoring

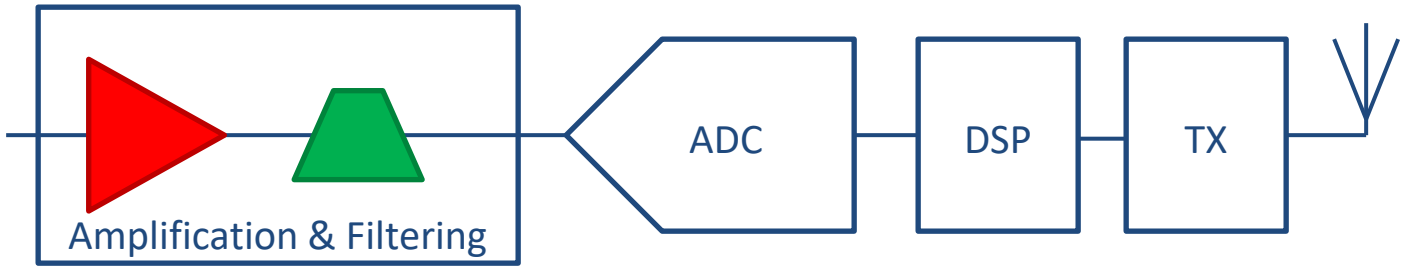
From large, inconvenient setups …

https://en.wikipedia.org/wiki/Electrocardiography

…. to small wearable devices



[Harpe, ISSCC 2015]

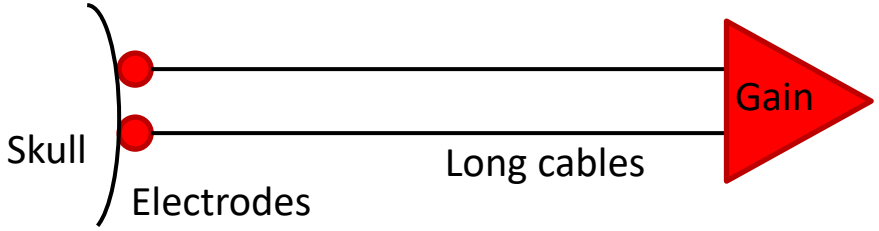


Note: check out the links in this presentation to learn more!

EEG Monitoring

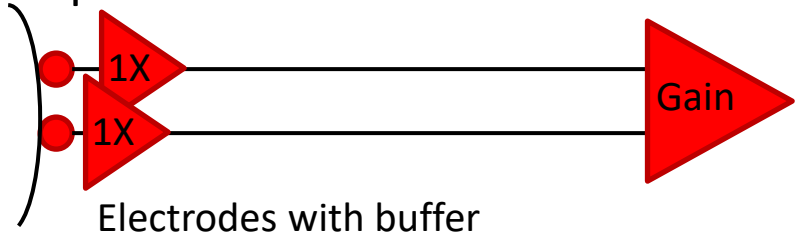
Passive electrode: high-impedance cable → sensitive to interference

https://en.wikipedia.org/wiki/Electroencephalography



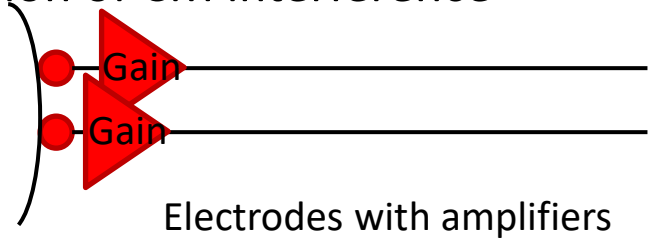
Active electrode: low-impedance cable → less sensitive to interference but additional power consumption and noise

https://www.youtube.com/watch?v=wdItWQDzeDE



Active electrode with gain: possible gain mismatch → CM to differential conversion → worse suppression of CM interference

https://www.youtube.com/watch?v=unkTiJoRTpc



Outline

- Introduction
- Biopotential interfaces
- Neural interfaces
- Other healthcare applications
- Examples from TU/e
- Summary

Neural Interfaces (or Neuroprosthetics)

- Interfaces that record and/or stimulate neural activity https://www.youtube.com/watch?v=K8uijjp6hfc
- This might apply to neurons in e.g.:
  - The brain (https://en.wikipedia.org/wiki/Deep_brain_stimulation)
  - Vagus nerve (https://en.wikipedia.org/wiki/Vagus_nerve_stimulation)
  - Spinal cord (https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/treating-pain-with-spinal-cord-stimulators)
  - Auditory nerve (https://en.wikipedia.org/wiki/Cochlear_implant)
  - Optic nerve/visual cortex/retina (https://en.wikipedia.org/wiki/Visual_prosthesis)

Neural Recording

- Similar to generic biopotential recording interfaces, but:
  - More stringent size/power requirements
  - Often array-based: MEA (Micro-Electrode Array) https://en.wikipedia.org/wiki/Microelectrode_array
  - Array is often multiplexed to lower-count interface electronics
    - E.g.: an array of 1024 electrodes might share 64 read-out channels
- Recording might include AP and/or LFP

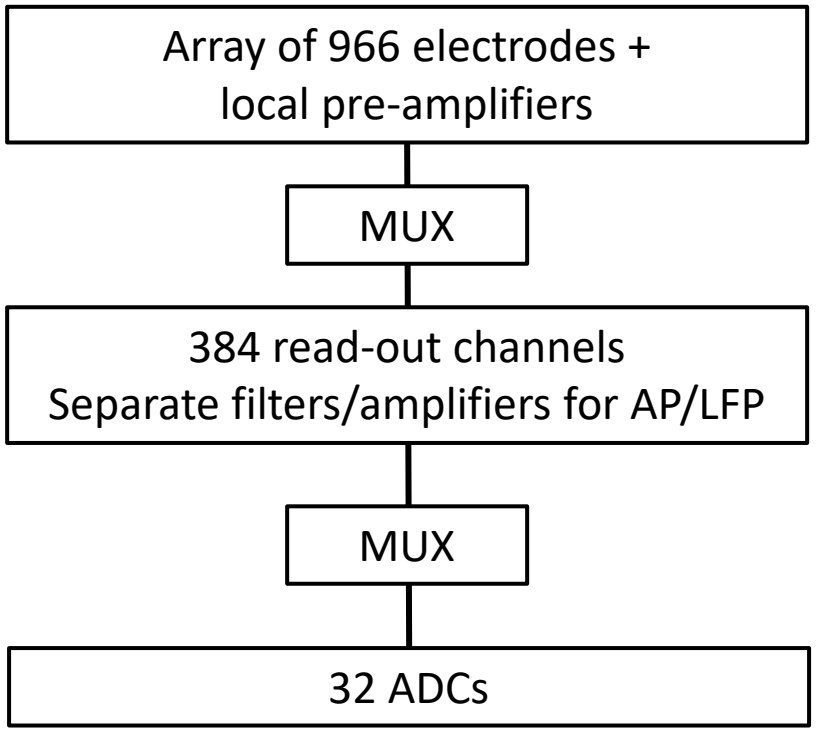
Type	Activity	Amplitude	Frequency
Action Potential (AP)	Single neuron	10µV – 100µV_{pp}	300Hz – 6kHz
Local Field Potential (LFP)	Cluster of neurons	0.1mV – 5mV_{pp}	0.5Hz – 200Hz

Neural Stimulation

- Affect the neural activity by means of a stimulation signal
- Can be done by means of electrical pulses, but is also possible by means of optics, ultrasound (FUS), magnetics (TMS)
- Electric: inject a pulse pattern
  - Current, voltage, charge-based
  - Charge balanced (Biphasic and symmetric)
  - Min level for stimulation, max level to avoid damage
  - Relatively high voltage may be required (10V +)

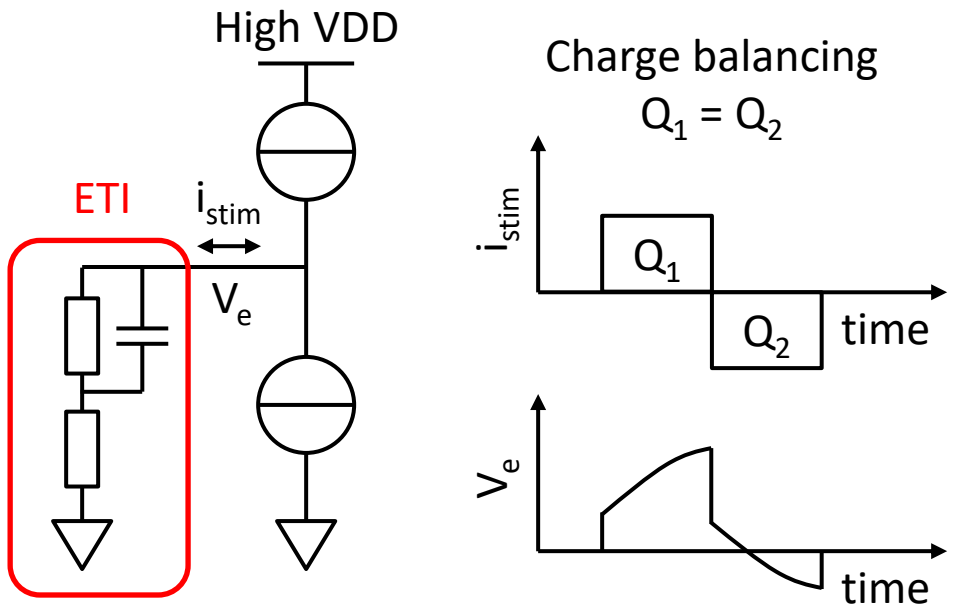
Neural Recording and Stimulation Interface

Neural recording



[C. Mora Lopez, et al., "A Neural Probe With Up to 966 Electrodes and Up to 384 Configurable Channels in 0.13 µm SOI CMOS," IEEE TBIOCAS, June 2017]

Neural stimulation

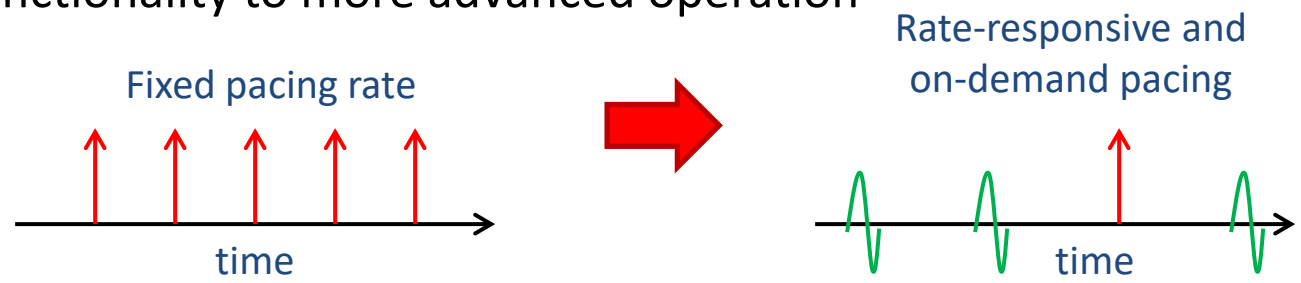


[Minkyu Je, Myung Hoon Sunwoo (editors), "Selected Topics in Biomedical Circuits and Systems," River Publishers]

(Cardiac) Pacemaker

- 1958: J.R. Pombo: External pacemaker with electrodes to the heart. 45kg, 12V car battery.
- 1958: Karolinska Institute, Sweden: fully implantable pacemaker. Lasted for 3 hours. Patient outlasted 26 pacemakers.

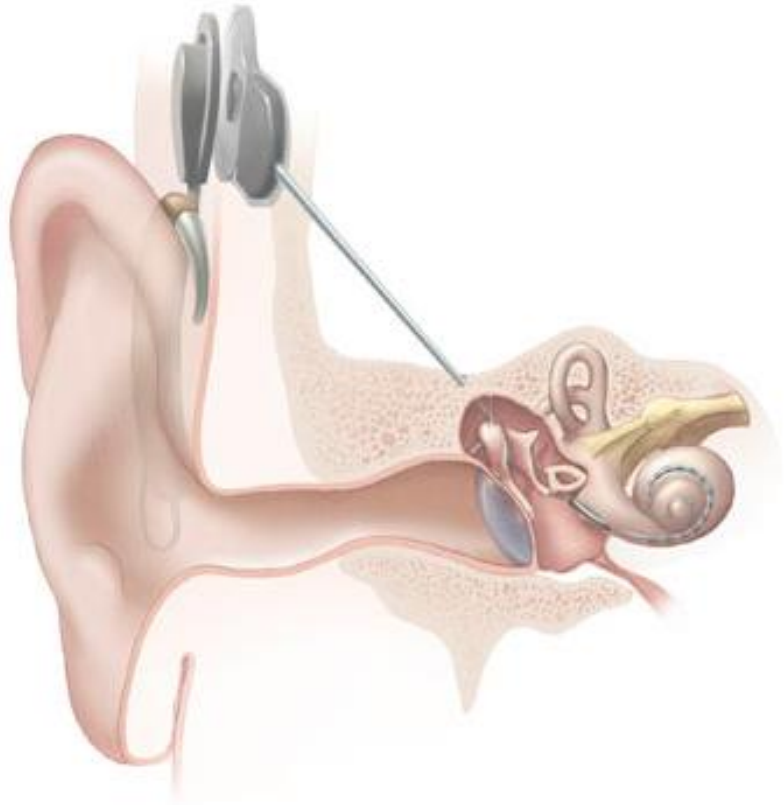
- Developments:
  - Device miniaturization
  - From basic functionality to more advanced operation



https://www.youtube.com/watch?v=SMXBR_YFocs

Cochlear Implant

- External components:
  - Microphone
  - Sound processor
    - Filter and prioritize sound
    - Personalization
  - RF coil (outside)
- Implanted components:
  - RF coil (implant)
    - Receive data from external coil
    - Receive energy from external coil
  - Electrodes to excite nerves
- Note: see book Sarpeshkar for more explanation



https://en.wikipedia.org/wiki/Cochlear_implant

Visual Prosthetics

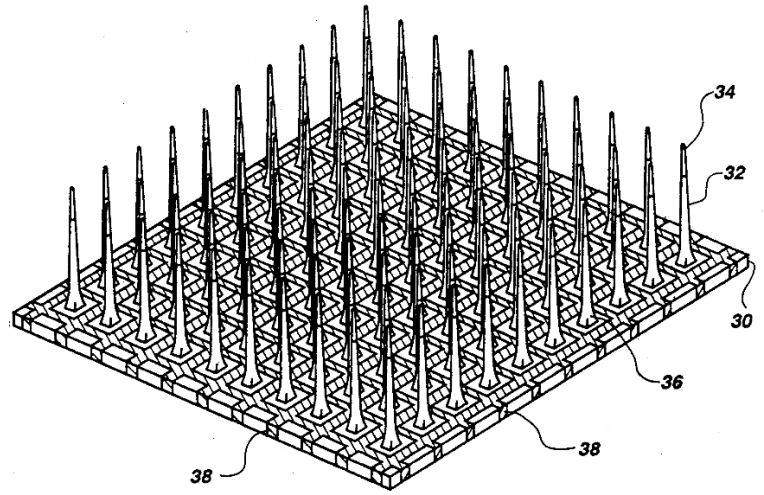
- Similar system as cochlear implant, but much more demanding (image sensor, processing, complexity)
  - An external image sensor captures vision
  - The signal is processed and transmitted through RF coils directly to the brains

http://www.youtube.com/watch?v=aeD7e0QfD2c

Deep Brain Stimulation

- A stimulation electrode area is placed in the brain, pointing at a specific area
- Stimulation can help in case of e.g.
  - Parkinson's disease
  - Movement disorders
- A few demonstrations:

Utah microelectrode array



http://www.youtube.com/watch?v=Uohp7luuwJI

http://www.youtube.com/watch?v=j3NjNKm0pio

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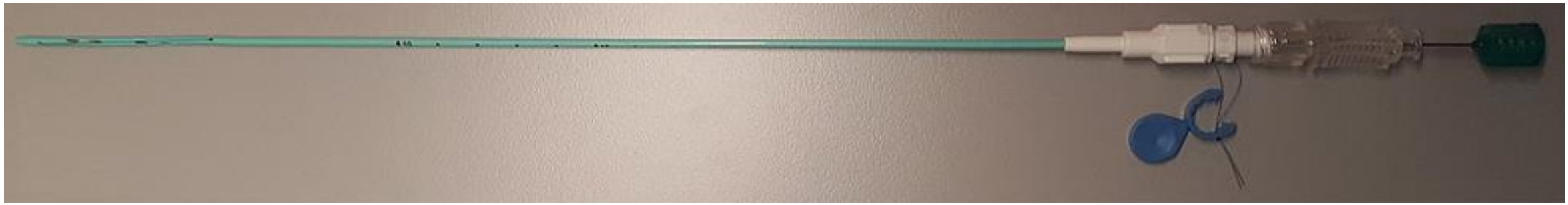
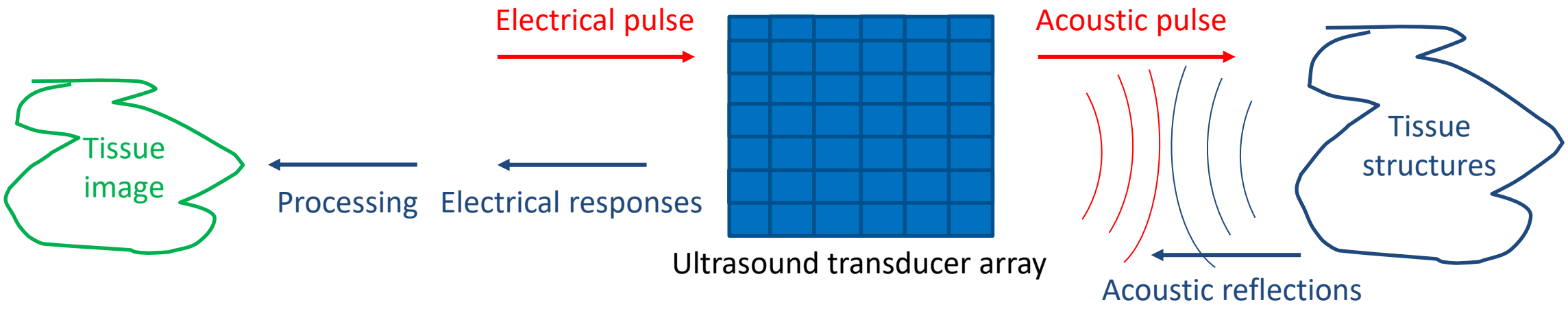
Ultrasound Catheters

- Medical imaging using a miniature ultrasound probe at the tip of a catheter
  - Image blood vessels (IVUS) or heart (ICE) to diagnose / locate stenosis





Intelligent Pills

- Application examples:
  - Medicine, released on demand
  - Sensors (pH, temperature, …)
  - Endoscopy (camera)
- Extra functionalities:
  - Remote control / wireless communication
  - Self propelling

https://www.youtube.com/watch?v=xLnjnZkK5x8

https://www.youtube.com/watch?v=X-jEhE10ZfY

Robotics

- Small “doctors”
  - Local medicine delivery
  - Cancer cell treatment
  - Diagnosis
  - Tissue repair

https://www.youtube.com/watch?v=ayteOA5VDRI

https://www.youtube.com/watch?v=Cg--UVL9xCc

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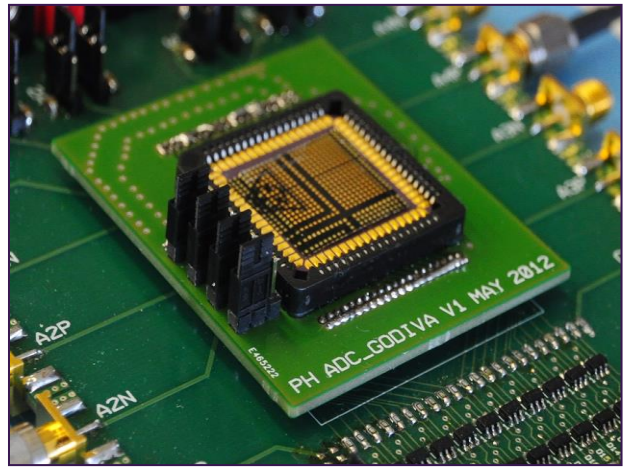
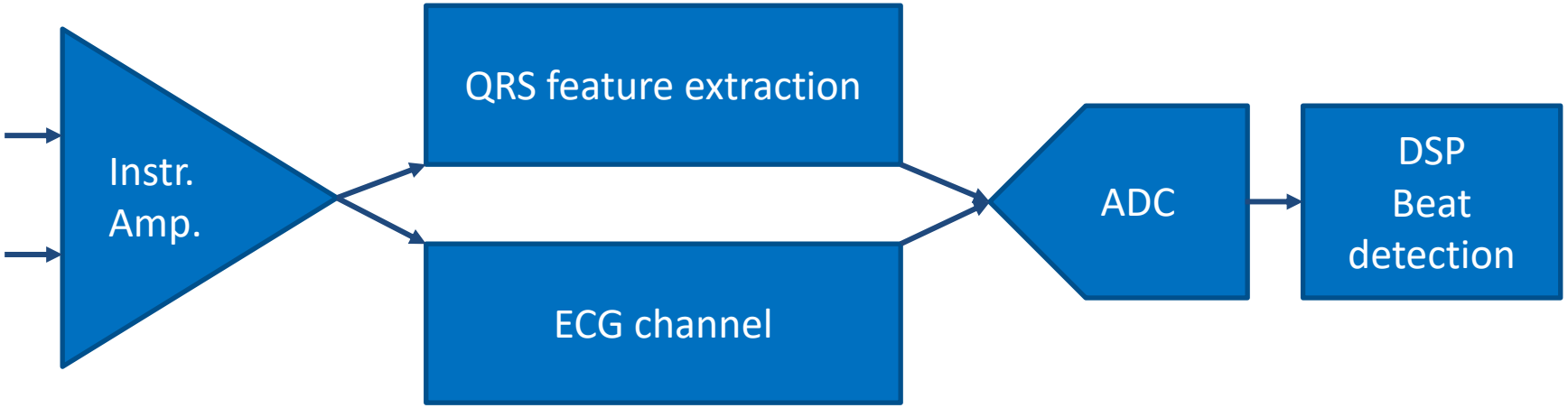
ECG Acquisition ASIC for Pacemaker Applications

- Single-chamber leadless pacemaker
- Heart-rate monitor

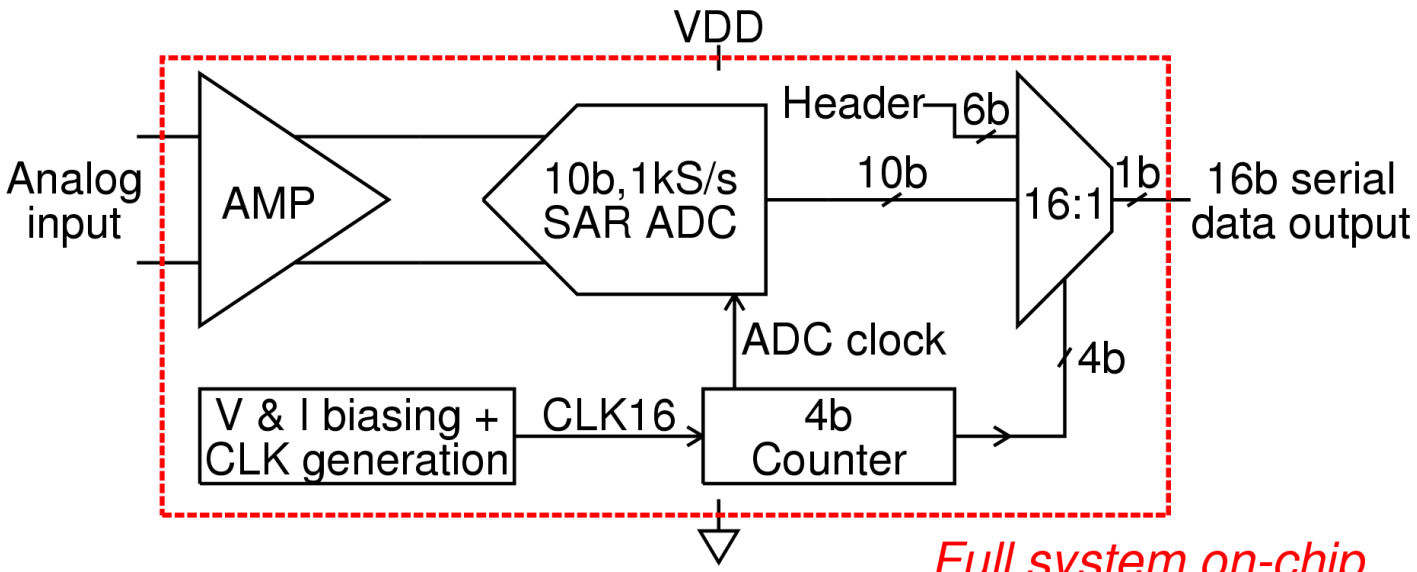


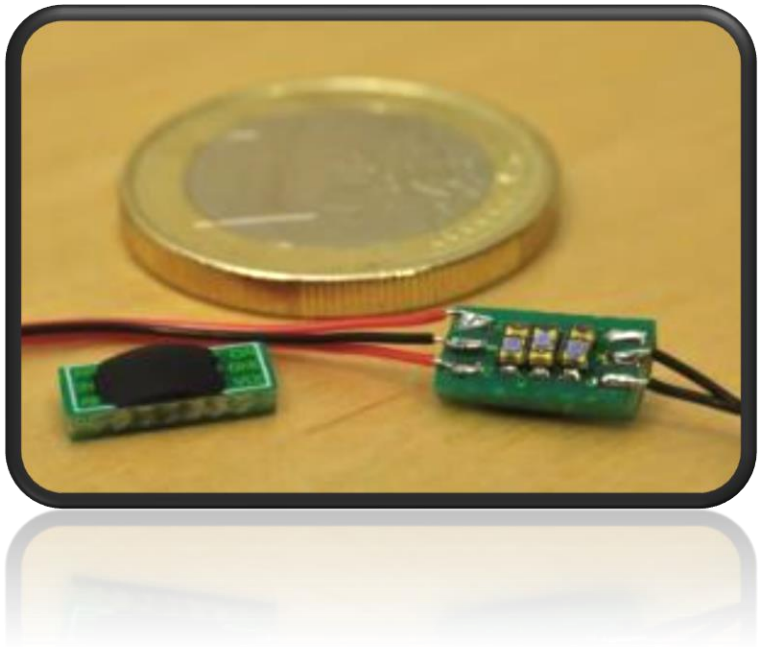


Long Yan, Pieter Harpe, Venkata Rajesh Pamula, Masato Osawa, Yasunari Harada, Kosei Tamiya, Chris Van Hoof, and Refet Firat Yazicioglu, "A 680 nA ECG Acquisition IC for Leadless Pacemaker Applications," IEEE Tran. Biomedical Circuits and Systems, Vol. 8, No. 6, 2014.

3nW ECG Recording Front-end

- Extremely low power ECG front-end





Pieter Harpe, Hao Gao, Rainier van Dommele, Eugenio Cantatore, and Arthur H. M. van Roermund, "A 0.20 mm^2 3 nW Signal Acquisition IC for Miniature Sensor Nodes in 65 nm CMOS," IEEE J. Solid-State Circuits, Vol. 51, No. 1, 2016.

This project was funded by the Dutch Technology Foundation (NWO).

32-Channel Digitizer for ICE Ultrasound Catheters

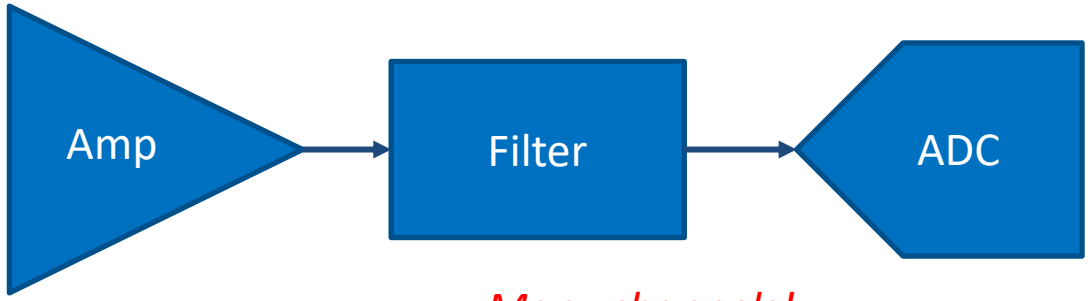
- Conventional: analog outputs → Many cables

Ultrasound transducer array

Grant no.: Ecsel-783132-Position-II-2017-IA
www.position-2.eu

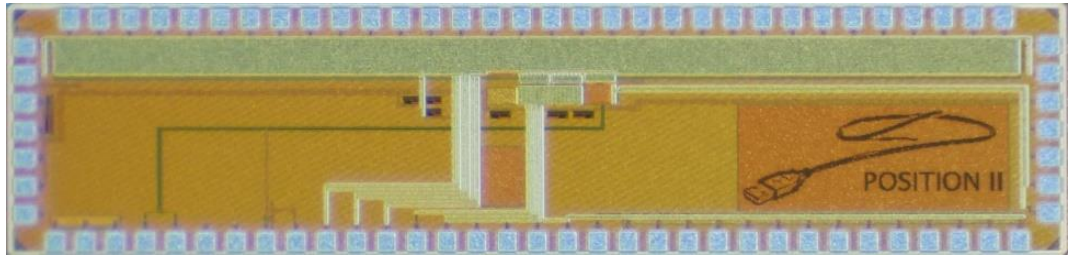
ECSEL Joint Undertaking

- Future: digitization at the tip → Few cables



Many channels!

In-probe digitizers for ultrasound catheters (ICE)



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Summary

- Healthcare trends & electronic requirements
- Biopotential and neural interfaces
  - Applications
  - Challenges
- Examples of active research in this field @ TU/e

Solution 1: ETI Impedance

a) Likely R_s and R_d will reduce, and C_d will increase.

b) This is like a plate capacitor, so $C_e = \varepsilon_0\varepsilon_r \cdot A / d$, with $\varepsilon_0 = 8.854\text{pF/m}$.
C_e increases proportional to A, and is inversely proportional to d.

c) Assuming that ε_r is 2 for cotton (you may find other values online):
$C_e = 8.854\text{p} \cdot 2 \cdot 16 \cdot 10^{-4} / 0.3\text{m} = 94\text{pF}$.

d) At 100Hz, the impedance of C_e is $Z_e = 1 / (2\pi 100 C_e) = 17\text{M}\Omega$. For 10% loss, the input impedance should be approximately 10x larger than Z_e, so 170MΩ.

Solution 2: Gain and Noise

a) $A \cdot (0.4mV_{pp} + 2mV_{pp}) + 50mV_{pp} = 1.2V_{pp} \rightarrow A = 479$ V/V (maximum gain).

b) $2\mu V_{rms}$.

Solution 3: Amplifier CMRR

a) A_c = 1mV / 50mV = 0.02 V/V.

b) CMRR = 20 $\log_{10}$ {A_d / |A_c|} = 20 $\log_{10}$ {100 / 0.02} = 74dB.

Solution 4: Electrode Mismatch CMRR

a) Substituting the equations from slide 28:

$V_{out} = A_d (V_+ - V_-) = A_d \{V_{cm} \cdot Z_{in} / (Z_{ETI1} + Z_{in}) - V_{cm} \cdot Z_{in} / (Z_{ETI2} + Z_{in})\}$

$V_{out} = A_d \cdot V_{cm} \cdot Z_{in} \{1 / (Z_{ETI1} + Z_{in}) - 1 / (Z_{ETI2} + Z_{in})\}$

This red term generates a differential output due to a common-mode input V_{cm}, so this can be modelled with a common-mode gain equation A_c, namely: $V_{out} = A_c V_{cm}$.

Equating the blue and red terms gives:

$A_d \cdot V_{cm} \cdot Z_{in} \{1 / (Z_{ETI1} + Z_{in}) - 1 / (Z_{ETI2} + Z_{in})\} = A_c V_{cm} \rightarrow$

$A_c = A_d \cdot Z_{in} \{1 / (Z_{ETI1} + Z_{in}) - 1 / (Z_{ETI2} + Z_{in})\}$

$CMRR = 20 \log_{10} \{A_d / |A_c|\} = 20 \log_{10} \{1 / Z_{in} \{1 / (Z_{ETI1} + Z_{in}) - 1 / (Z_{ETI2} + Z_{in})\}\} \rightarrow$

$CMRR = 20 \log_{10} \{(Z_{ETI1} + Z_{in}) (Z_{ETI2} + Z_{in}) / \{Z_{in} (Z_{ETI2} - Z_{ETI1})\}\}$

Under the assumption that $Z_{in} >> Z_{ETI}$, this simplifies to:

$CMRR \approx 20 \log_{10} \{Z_{in}^2 / \{Z_{in} (Z_{ETI2} - Z_{ETI1})\}\} = 20 \log_{10} \{Z_{in} / \Delta Z_{ETI}\}$

b) $CMRR \approx 20 \log_{10} \{Z_{in} / \Delta Z_{ETI}\} \rightarrow 80dB = 20 \log_{10} \{Z_{in} / 40k\Omega\} \rightarrow Z_{in} = 400M\Omega$.

Solution 5: Dynamic Range

a) A signal with $0.4mV_{pp}$ amplitude has an RMS value of $0.14mV_{rms}$ (assuming a sine wave). So, the DR is $20 \log_{10} (0.14mV_{rms} / 2\mu V_{rms}) = 37dB$.

b) Because of the 60dB CMRR, the $100mV_{pp}$ CM input signal is equivalent to a $0.1mV_{pp}$ differential input signal. Together with the EEG signal ($0.4mV_{pp}$) and the disturbance ($2mV_{pp}$), that gives $2.5mV_{pp}$, resulting in $0.9mV_{rms}$.
The DR is now $20 \log_{10} (0.9mV_{rms} / 2\mu V_{rms}) = 53dB$.

Solution 6: Interference Sensitivity

a) Because Z_{in} can be ignored compared to Z_{out} (10x larger, so negligible):
$V_{if2} = V_{if} \cdot Z_{out} / (Z_{out} + (1/sC_{if})) = V_{if} \cdot sC_{if} \cdot Z_{out} / (sC_{if} \cdot Z_{out} + 1)$
Interferences at higher frequencies have more impact, because Z_{if} becomes smaller due to its capacitive nature, giving more coupling from the interference source to the system. We can also see that from the above equation of the transfer function.

b) $|V_{if2}| = |V_{if} \cdot sC_{if}Z_{out} / (sC_{if}Z_{out} + 1)| = 2 \cdot (2\pi 1k) \cdot 2p \cdot 500k / \sqrt{(((2\pi 1k) \cdot 2p \cdot 500k)^2 + 1)}$
$|V_{if2}| = 13mV$.

c) Approximately 10x lower, so 1.3mV.

Solution 7: AC Coupling

a) For 1dB loss, Z_{in} should be about 8x higher than Z_{ETI}, so 4MΩ, as the loss is given by $20 \log_{10} (Z_{in} / (Z_{in} + Z_{ETI})) = 20 \log_{10} (8 / (8 + 1)) = -1\text{dB}$.

b) Z_{in} is given by $1 / sC_1$, so the lowest impedance is achieved for the highest frequency → $|1 / sC_1| = 8\, Z_{ETI}$ at 500Hz, so: $1 / (2\pi 500 \cdot C_1) = 4\text{M}\Omega$ → $C_1 = 80\text{pF}$.

c) C_2 follows from the gain requirement: $A = C_1 / C_2$ → $C_2 = 800\text{fF}$.
R follows from the cut-off frequency: $f_c = 1 / (2\pi RC_2)$ → $R = 2\text{T}\Omega$.

Note: R is excessively large, so this shows the problematic trade-offs in this design.

Solution 8: DC Coupling

a) To deal with the 100mV DC level instead of the 400µV signal only, the DR has to be expanded by 20 $\log_{10}$ (100mV / 400µV) = 48dB.

b) With DC coupling, the maximum gain is 10 V/V (limited by the DC level).
With AC coupling, the maximum gain is 2500 V/V (set by the signal only).

Note: the increase of gain (from 10 to 2500 V/V) is also 48dB, matching the DR change.